EYE RESEARCH

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# eye research

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# preface

New drugs, new surgical techniques, and a better understanding of the anatomy and physiology of the eye have brought many potentially blinding disorders under control during the past few decades. Even so, 30,000 or more Americans lose their eyesight every year. Almost 1 million persons in the Nation cannot read newsprint even with the aid of glasses, and some 400,000 are legally blind.

The National Institute of Neurological Diseases and Blindness was formed in 1951 to conduct and support research on neurological and sensory disorders, including those which lead to blindness. It is one of the National Institutes of Health, the research arm of the Public Health Service.

The Institute's broad program of research and training is helping to combat blinding diseases as glaucoma, cataract, uveitis, and disorders of the cornea and retina. Research gains of recent years and something of the size of the problem that lies ahead are described in this booklet.

# contents

Page
Preface 1
Introduction 4
Cataracts 6
Glaucoma 9
Retinal Detachment 14
Retinitis Pigmentosa 17
Diabetic Retinopathy and Other Vascular Disorders 19
Other Retinal Disorders (including Color Vision) 22
Disorders of the Cornea 24
Uveitis 28
Trachoma 31
Refractive Errors 34
Amblyopia Ex Anopsia 37
Eye Injuries and Tumors 39
The Future 42

*Eye surgery. (Columbia University)*

# introduction

Man's search for the causes of blindness has been going on for centuries. Prehistoric man considered the eye to have magical powers for both good and evil. Because of this belief and because of the accessibility of the eye for examination and therapy, ocular problems have occupied physicians through the ages.

In spite of this heightened attention to the diseases and afflictions of the eye, the causes of blindness are still largely unknown to science. Modern methods of early detection, diagnosis, and treatment of diseases are saving the sight of many people, but still many become blind each year from disorders that could probably be prevented through scientific research.

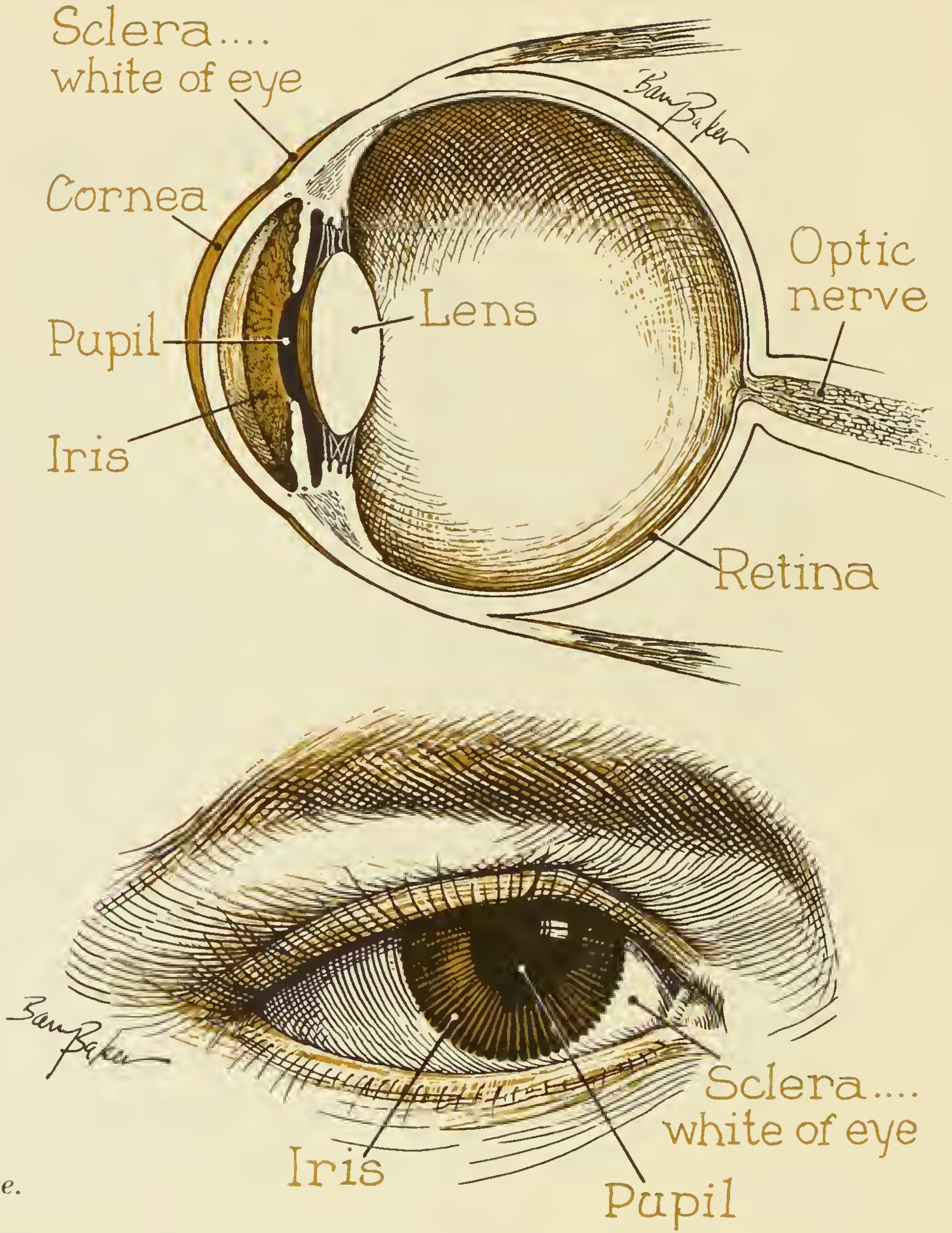
Advances made possible by the research and training programs of the National Institute of Neurological Diseases and Blindness have saved many patients from blindness. Glaucoma, strongly suspected as an inherited disorder, has yielded to early detection and treatment which prevents blindness in most cases. Some viral infections of the cornea can now be successfully treated with drugs. Other types of visual loss which might result from drug treatment for other diseases can now be prevented by close medical supervision.

These and other research gains since the start of the Institute have spared patients and their families much heartache and disappointment, and have also saved the Nation thousands of dollars in care for the blind.

Nevertheless, we have only begun to acquire the knowledge necessary to combat some of the more complex problems of vision. The degenerative disorders of aging, closely associated with natural growth and aging processes, are among chief causes of the continuing increase in blindness. Although these and other ocular disorders will challenge researchers to find their cure, dividends to be expected from study of eye diseases go far beyond the eye itself.

For example, investigation of cataracts leads to information on the growth and aging process of all cells. The blood vessels in the eye can be seen and examined with ease and may be an index to vascular diseases in other parts of the body. For years, the eye's cornea has provided the researcher with fertile ground for the study of viruses and other infections. The uvea (formed by the iris, choroid, and ciliary body) is an excellent site to study immunology. Many general diseases are discovered first in the eye. In others, the eye manifestations come later, but there is often a close relation, as in diabetes, rubella (German measles), and diseases of the nervous system.

Not all eye disorders can be discussed in a brochure this size, but most will fall into one of the following categories.



*The outer eye, main parts, and cross section of the eye.*

# cataracts

A cataract is a cloudiness of the lens of the eye which interferes with the normal passage of light rays through the pupil. While the cloudiness of the lens cannot be cured, the lens can be removed. In recent years the use of an enzyme called alpha-chymotrypsin has made the removal of some cataracts easier by weakening the ligaments holding the lens capsule in place. Cataract operations are 98 percent successful with vision restored to 20/30 or better in 85 percent of the cases.

Cataracts are the leading cause of blindness in the United States today. They occur more often among people over 55 than in younger persons. As the life span increases, more people are expected to have cataracts.

## what are cataracts?

A cataract is not a film growing over the lens, but a change in the lens itself. If you think of the normal lens of the eye resembling the white of a raw egg, which is transparent and can be seen through, then a cataract resembles the white of a cooked egg which is opaque and cannot be seen through.

Progressively blurred vision is the principal symptom. There is no pain. Paradoxically, although distant vision is blurred in the beginning stages of the cataract, near vision is somewhat improved. Consequently, these patients temporarily read better without glasses.

Of the different types of cataracts, the most common is the "senile" or "over 55" cataract associated with an increase in soluble protein of the lens. Scientists believe that this type of cataract is related to, though not a necessary part of, the aging process.

Some children are born with cataracts. A pregnant woman who has German measles before the third month of her pregnancy endangers the sight of her infant. Diabetes and other metabolic defects, radiation exposure, and injuries to the lens may also cause cataracts. Cataracts resulting from other eye disorders are called "secondary cataracts."

## treatment

Several decades ago operations were only attempted when the cataract had "ripened." This is no longer true. Now a decision as to when the operation is performed depends to a large extent upon the patient's visual requirements. For example, the doctor may recommend an earlier removal for a person who uses his eyes extensively in his profession than for a housewife.

Often the condition of the other eye affects the doctor's recommendation about cataract removal. If vision is already impaired in one eye, a cataract which forms on the remaining eye must be removed early to give the patient one usable eye.

Removal of the lens results in certain disadvantages to the patient. Eyeglasses may enable him to move around normally and to read, but they do not take the place of the natural lens. Some side vision is lost. Also, the operated eye is very farsighted. Glasses, placed in front of the eye, magnify an object considerably. If there is a cataract in only one lens and it is removed, the image seen by the operated eye and the normal eye may not fuse. For this reason, physicians sometimes recommend waiting until a cataract develops in the second eye and justifies the removal of both lenses.

Contact lenses fitted to the eye close to the site of the original lens can correct vision without objectionable magnification of the image. Some persons, however, have difficulty adjusting to contact lenses.

Sometimes cataracts conceal defects of other parts of the eye which are not apparent before the lens is removed. A simple cataract operation, however, is one of the safest performed. Children born with cataracts may retain adequate vision without surgery. However, surgery may be unavoidable.

# research

What causes cataracts? The cells of the lens, which are essentially protein, are kept alive by energy from the breakdown of carbohydrate. A cataract forms because of changes in the protein structure of the lens and its carbohydrate metabolism.

A number of different factors appear to be involved. The higher-than-normal incidence of cataracts in diabetics is one of the many proofs of a relationship between cataracts and the way the body uses sugar, especially glucose.

Institute grantees recently helped put forth a new and important theory on the formation of some types of cataracts. This theory suggests that a form of sugar penetrates the lens fibers and is reduced to its alcohol derivative. In this form it cannot diffuse out of the fibers or be metabolized, and thus it becomes locked in the lens. As the concentration of the alcohol derivative increases, water moves into the lens by osmosis, causing swelling, bursting, and eventual disintegration of the fibers.

In an effort to clarify the mechanism for the buildup of insoluble proteins in cataracts, biochemists have made exhaustive studies of amino acids, the building blocks of proteins. They found that amino acids and potassium are actively transported into the lens, and sodium out of the lens, by carrier systems located in the front outer layer (epithelium). Movement of water and other products between lens and its surrounding tissues occurs passively through diffusion. A defect in the transport mechanism for getting amino acids into the lens may be responsible for cataracts associated with diabetes.

While chemists have studied lens chemistry, other research specialists have observed changes in the individual cells of the lens, particularly those changes produced by radiation. To understand the abnormal process which takes place during cataract formation, scientists have studied the life span of cells to learn how they multiply and their characteristics under the high magnification of the electron microscope.

Research must continue until scientists discover which controllable changes in body chemistry produce cataracts. They hope that new insights into a range of biochemical factors connected with the lens will enable them to deal more effectively with the problem.

# glaucoma

Glaucoma, increased pressure within the globe of the eye, is the second leading cause of blindness in the United States today. Although it cannot be cured or prevented, visual loss can be avoided by early diagnosis and proper treatment.

But early diagnosis is often hampered by lack of symptoms. Some forms of glaucoma steal sight so slowly and painlessly that many people do not realize they have the disorder until irreparable damage is done.

## what causes it?

Institute-supported research, as well as research by other scientists, has been accumulating evidence that primary glaucoma (that not caused by another disease) is inherited. Offspring of glaucoma patients may be carriers and pass the gene on to their children without getting the disorder themselves.

This new knowledge will alert physicians to look for early signs of glaucoma in relatives of people who have the disorder. Family physicians, internists, and ophthalmologists now often include an eye pressure (tonometer) test in routine medical examinations. Early care helps guard against visual loss.

## what is it?

In glaucoma, the watery fluid, which normally flows through the eye, fails to drain out as readily as in the normal eye. Therefore, the pressure builds up and destroys the nerve fibers of the retina and optic nerve and blood vessels feeding these tissues. Improved treatment and better methods of measuring intraocular pressure now make it possible to recognize and control most glaucoma. If drugs fail to keep the pressure down, surgery can be performed to create another outlet for the fluid.

## types of glaucoma

**Infantile.**—Infantile glaucoma, also called congenital, occurs at birth or during the first years of life. It is inherited as an autosomal (non-sex connected) recessive trait. If untreated, blindness occurs early, but surgery is often effective and can be repeated, if necessary. The best safeguard is regular pediatric examination.

**Acute Glaucoma.**—Surgery is the standard treatment for primary acute glaucoma. Here, the pressure inside the eye mounts to a dangerous level in a matter of hours, usually causing an excruciating headache and vomiting. The pressure must be reduced immediately or blindness may result. If a sector of the iris, the colored part of the eye, is removed, outflow of fluid from the eye is facilitated. Urea, mannitol, glycerol, or other chemicals which rapidly (but temporarily) reduce the volume of fluid in the eye may also be used. This form is sometimes called angle-closure glaucoma. It is caused by blockage of the outflow channels in the anterior chamber angle—the point through which fluid flows out of the eye. It occurs in persons in whom the anterior chamber angle has always been narrow. Acute glaucoma presents an immediate hazard, but it can almost always be brought under control if treatment is sought promptly.

**Chronic Glaucoma.**—Chronic glaucoma presents a different picture because its victim is usually unaware

*An animal eye furnishes valuable data in understanding glaucoma.*

of symptoms. Therefore the greatest problem in this type involves detecting the disorder so that sight-saving treatment can be started.

**Secondary Glaucoma.**—Secondary glaucoma may be caused by other conditions in the eye, such as cataract or dislocation of the lens, infection, injury, and surgery.

## detection

Diagnosis of glaucoma depends on instruments which measure the intraocular pressure. The most common of these is a small hand instrument called the Schiotz tonometer. Research has increased the reliability of the Schiotz tonometer. But eye pressure, like blood pressure, varies from day to day and at various hours during the day. The first tonometer reading may show a raised pressure because of squeezing of the eye. For this reason, if the doctor gets a higher than normal eye pressure measurement, he does not immediately assume the patient has glaucoma, but asks him to return for another pressure reading. By the same token, a normal pressure reading does not necessarily mean an absence of glaucoma.

Sometimes it is necessary for the patient to enter the hospital for pressure measurements at repeated intervals throughout the day. In this case the doctor may use other instruments and techniques. The applanation tonometer, a large instrument on a stand, measures pressure more accurately than the Schiotz tonometer. Another technique, tonography, provides a 4-minute continuous recording of outflow. In addition, the physician sometimes measures the eye pressure before and after drinking large amounts of water.

## treatment

Measurement of intraocular pressure is important not only for diagnosis of glaucoma but also for evaluating treatment. A variety of drugs in the form of eye drops are administered to keep the pressure at normal levels and thereby prevent damage to eye tissues.

## research

Research studies, which add to our knowledge of glaucoma, are making treatment of the disorder more effective.

Until recently, doctors concentrated on screening surveys to detect glaucoma in persons over 40. Now they have begun to think in terms of detecting a susceptibility to glaucoma at an early age before any permanent changes have resulted in the eye. These experiments indicate that even in childhood, a tendency towards the disease may be detected through the local use of steroid drops. The elevated pressure decreases when the drops are withdrawn, so vision is undamaged.

Research also has enhanced understanding of the mechanisms that control the flow of fluid through the eye. Interference in the outflow channels has been found the primary cause of the increased eye pressure. Drugs can facilitate fluid outflow or decrease fluid production, but scientists ultimately hope to prevent the outflow channels from becoming defective. They believe research will bring the medical world closer to preventing all damage from increased pressure in the eye.

*NINDB scientists' recordings from an enucleated cat eye contribute to understanding of the basic causes of glaucoma.*

# retinal detachment

Retinal detachment is a separation of the innermost layer of the eye, the retina, from the choroid, the layer just behind it. These two layers are usually in close contact; but if the retina should peel away or be pushed up from the choroid, all or part of the vision is blacked out.

## what causes it?

Retinal detachment may be due to injury or disease. Changes that occur with old age increase the chances for retinal detachment. Persons who are nearsighted or who have had cataract operations may also be predisposed to detachment. Most detachments occur for reasons unknown to medical science.

The retina is most often detached when a tear or hole develops in its substance. Fluid seeps through this tear from the vitreous, the jellylike body that fills the interior of the eyeball. This fluid gets behind the retina and separates it from the choroid. The same effect may be caused by extra fluid which accumulates because of an infection in the area or vascular disturbance. The retina can also be detached by scarlike strands in the vitreous or by tumors in the eye.

## symptoms

Retinal detachment has been described as a curtain being drawn across the eyes. Other symptoms, such as seeing sootlike spots or light flashes, may be signs of tears in the retina or changes in the vitreous which may lead to detachment.

## treatment

If the retinal detachment is diagnosed in its early stages, patients may benefit from exciting advances in eye research, making it possible to reattach the retina and restore vision. With good care, 85 percent of the cases can achieve reattachment. If untreated, the detachment becomes complete and permanent blindness results.

**Scleral buckling.**—One surgical technique is called scleral buckling and involves removing a strip or cutting a flap from part of the sclera, the tough outermost layer of the eye. By pinching the cut part, the eyeball is made shorter. This shortening has the effect of pulling the choroid and the retina close together.

Other, older, techniques are designed to create small burns on the retina or choroid. These injuries form scar tissue that acts as a bond between the two layers.

**Diathermy.**—One such method, known as diathermy, uses a small electrode to penetrate the sclera and produce a burn on the choroid. The burn forms scar tissue which welds the choroid to the retina.

**Photocoagulation.**—Another method, known as photocoagulation, uses light rather than heat to produce a burn. Light of the intensity of sunlight is focused into the eye through the pupil, producing a burn on the choroid and retina. Tissue changes known as coagulation, similar to the coagulation of blood when it clots, spot-weld the retina.

Although light coagulation can be used to treat minor detachments, it is used more often to prevent retinal detachments by surrounding tears or holes in the retina by adhesions before it becomes detached.

## research

Two new techniques have been developed but they are still in the experimental stage. One is a refinement of photocoagulation using "lasers," devices which can produce narrow, intensified light rays up to one thousand times the strength of sunlight. Using lasers, the beam of light need be on for only one-thousandth of a second to produce pinpoint burns on the choroid and retina. This kind of "knifeless surgery" produces even less discomfort to the patient than photocoagulation.

Another new treatment is the use of liquid silicone, an inactive chemical, to replace the vitreous fluid in the eye. The transparent silicone remains in liquid form and helps hold the retina in contact with the choroid. This technique has recently been used to cure retinal detachments previously considered hopeless.

Research is proceeding to perfect existing treatments for retinal detachments, to develop new treatments, and to gain a greater understanding of the causes of this disorder so that it may be prevented.

*Recording from a single cell in the retina of the horseshoe crab promotes understanding of color vision.*

# retinitis pigmentosa

Retinitis pigmentosa is an inherited disease that usually produces its first symptom—night blindness—in childhood. Over the period of a lifetime the disease gradually decreases the ability to see at night and cuts down more and more on the amount of side vision, until the effect is similar to that of blinders used on horses, or what has been called "gun barrel vision." This loss is caused by changes in the retina, the innermost layer of the eye which receives light and generates nerve impulses.

## treatment

Although there is no known treatment that can halt the progress of retinitis pigmentosa in a person who has the gene for this disease, it is not a hopeless condition. Many patients keep their reading vision throughout their lives, although it may be restricted to a small central part of the visual field. Only a small number of cases result in total blindness.

The disease can be diagnosed by an ophthalmologist using an instrument called an ophthalmoscope. Looking into the interior of the eye, if the disease is present, he can see many black pigment deposits scattered throughout the retina, but particularly around its edges. This extra pigment is characteristic of the disease, as the name *retinitis pigmentosa* suggests, but in rare cases the pigment may be absent.

## research

A useful tool that enables scientists to distinguish retinitis pigmentosa from other diseases of the retina is the electroretinogram (ERG). This device records electrical impulses that the retina gives off when light strikes it. Electronic computers used with the ERG help pick up even the weakest electrical signals of a retina damaged by retinitis pigmentosa.

Many scientists are conducting research to find out how retinitis pigmentosa affects retinal tissue. They have observed that the rods and cones, which are the specialized light-receiving cells of the retina, become less active. Those used for peripheral or side vision are particularly affected. Because there is greater damage to the rods, which are used to detect shades of black and white in dim light, night vision is also damaged.

The deteriorated light-receptor cells are replaced by an overgrowth of the supporting connective tissue. The invasion of connective tissue accompanies atrophy, or wasting away, of the blood vessels and the part of the optic nerve that passes through the retina. This atrophy further damages the ability of the retina to function.

Why these changes occur is still unknown. There is evidence that some abnormality in the biochemistry of the eye or of the body's metabolism may be responsible. Some scientists think the disease is due primarily to a change in the pigment-producing tissue of the retina, or to changes in the small blood vessels that supply nourishment to the outer layers of the retina. Once the cause of retinitis pigmentosa is pinpointed through research, it may be possible to find ways to prevent the disease or stop its progress.

Institute grantees have mapped out the retinal changes occurring in rats, mice, and dogs with inherited diseases resembling retinitis pigmentosa in man. The close resemblance of retinitis pigmentosa to night blindness caused by vitamin-A deficiency suggested that it, too, might involve a local abnormality in the vitamin-A metabolism. However, while administration of vitamin-A supplements improved vitamin-A deficient night blindness, it had no effect on retinitis pigmentosa. Furthermore, studies revealed basic differences in the early chemical changes in the retinas of animals with the two disorders.

Institute scientists have been able to retard some forms of retinal degeneration by keeping the animal in dim light. The finding suggests the possibility that the use of dim light in patients with retinitis pigmentosa might protect the eyes.

# diabetic retinopathy and other vascular disorders

Diabetic retinopathy is a degenerative disorder of the retina which occurs as a complication of diabetes. It accounts for 8.4 percent of all blindness in the United States. Discovery of insulin and other similar products has improved the well-being and life-expectancy of diabetic patients, but the complications of the disease have increased.

Why do some diabetics develop this eye complication while others do not? Some authorities believe that those diabetics who have been kept in strict control are less prone to develop diabetic retinopathy, since 75 percent of the disorder's victims have been lax in their control or followed a so-called "free" diet. Another 25 percent, however, developed the retinal damage in spite of good diet, good hygiene, and proper amounts of insulin or its oral equivalent.

## what is diabetic retinopathy?

Diabetic retinopathy is related to and probably stems from the same body defect as diabetes, a disturbance of carbohydrate and fat metabolism. In this condition the body is unable to properly utilize and store glucose, a form of sugar.

In some diabetics, degeneration causes ballooning of the small blood vessels of the retina. These ballooning, or aneurysms, resemble diabetic-caused blood vessel changes in the kidneys. In later stages diabetic retinopathy consists of retinal exudates, hemorrhages, and possibly retinal detachment.

## treatment

Until a few years ago, once the blinding process of diabetic retinopathy began, it usually progressed. Recently, however, a few physicians have had success with removal of the pituitary gland in patients threatened with blindness. Such patients are followed closely for the appearance of adverse effects of the operation. Preliminary results have shown no harmful effects from the surgery, but further observations are needed before the procedure can be widely recommended.

## research

The electron microscope and special staining techniques have aided laboratory scientists in describing the structure and chemical composition of the small blood vessels, called capillaries, in which the aneurysms occur. Such basic studies have distinguished the diabetic changes in these capillaries from similar damage of hypertension and arteriosclerosis, which often occur at the same time.

Because animals with diabetes do not usually develop the retinopathy, scientists studying this condition have lacked an experimental model. Recently, investigators have discovered that some diabetic dogs do develop retinal changes comparable to those in humans. They have accumulated some 50 such animals and hope to obtain more through veterinarians and dog owners alert to their potential contribution to science. Study of these dogs will help determine whether the lesions are a result of diabetes or of some genetic or other disorder attending diabetes.

Investigators who examined 1,000 eyes removed at autopsy, 300 of which were from diabetic patients, concluded that diabetic retinopathy may result from degeneration of all parts of the retina, rather than just the blood vessels.

Research on the circulation of blood through the eye has been aided by a recently developed technique for dissolving the tissues surrounding the blood vessels in the retina of the eye removed at autopsy.

Microscopic examination of the retinal vessels isolated by this technique has now led to the first attempt to explain the mechanism of diabetic retinopathy. According to this theory, "mural" cells in the wall of the capillaries die, causing some capillaries to lose their tone and become oversized. This permits an excess flow through certain channels, while other areas are bypassed. The rerouting of blood flow in turn results in distension of some capillaries in the form of aneurysms.

Understanding how diabetes causes capillary aneurysms does not prevent or cure diabetic retinopathy, but it is a necessary first step toward such control.

## other vascular disorders

Diabetic retinopathy is only one of the vascular disorders that affect the eye. Diseases of the eye's blood vessels cause some of the most baffling cases of blindness. Tiny clots or hemorrhages that might go unnoticed in another part of the body may cause serious loss of vision in the eye.

Photocoagulation techniques, including the laser beam (see Other Retinal Disorders) have recently proved helpful in treating vascular disorders, especially blood vessel tumors of the eye. A substance called fibrinolysin is reported by some to be useful in dissolving blood clots in the retina.

Research studies to better understand the normal and abnormal blood circulation in the eye may provide more effective means of treating these vascular disorders.

*Dissecting microscope aids in cutting ultra thin sections for viewing under the electron microscope.*

# other retinal disorders

Although the cornea, lens, and other tissues help convey light through the eye, the actual visual process does not begin until light strikes the retina. This light-sensitive lining at the back of the globe is the site of many visual disturbances. Affections of the retina include congenital anomalies, injuries, inflammations, circulatory disturbances, degenerations, detachment of the retina and tumors.

Many of these disorders, especially degenerations and anomalies existing at birth (congenital) are untreatable by present-day medicine. Therefore, investigators are hard at work to understand the basic anatomy and function of the retina, which they feel is necessary before treatment or prevention is possible.

These investigations have helped explain the workings of the rods and cones, tiny components of the retina which absorb light. The rods are concerned with vision in dim light and at night, and communicate only sensations of gray. The cones are the receptors of color vision. Both rods and cones contain visual pigments which bleach when light strikes them; this bleaching reaction is the first step in the process by which a nerve impulse is sent to the brain to register a visual image.

## color vision

Using delicate and supersensitive instruments, scientists are searching out the secrets of how man sees colors. They have found, for instance, that color blindness may be due to either one of two causes: one, the eyes may lack one of the three (red, green, or blue) color-sensitive pigments or; two, they may have all the required pigments but two of them may override the third to produce a color-confused sensation.

## examination of the retina

Many eye diseases can be diagnosed by characteristic changes in the appearance of the retina, which the ophthalmologist sees by peering into the eye with an ophthalmoscope.

Observations with the ophthalmoscope are supplemented by measurements of visual function, such as visual acuity, visual fields, dark adaptation, and color vision. Since many of these tests require a response from the patient, they are difficult to administer to small children, mentally disturbed patients, and others who, for one reason or another, are unable or unwilling to cooperate. Thus, attempts have been made to substitute "objective" type tests which do not require a response from the patient.

## the electroretinogram

One of these tests is the electroretinogram (ERG), which uses an electrode attached to a contact lens to measure the electrical response of the eye to a blinking light.

The ERG has undergone several refinements and can now be used to determine which parts of the retina are functioning normally and which are damaged by disease or injury. It aids in the diagnosis of such diseases as retinitis pigmentosa, Leber's amaurosis congenita, congenital retinal dysfunction, Tay-Sachs disease, congenital achromatopsia, and early macular degeneration.

# disorders of the cornea

The cornea is a transparent membrane covering the iris or colored portion of the eye. Similar in size and structure to the crystal of a wristwatch, it acts as a protective window through which light rays pass on their way to the retina. The cornea also helps to bend and focus light rays.

Scarring produced by injury and corneal ulcers causes 10 percent of the blindness in the United States and much more of the blindness in the Near and Far East. However, new drugs and improved treatments are helping to reduce the amount of this type of blindness.

## different causes

Doctors usually classify corneal ulcers by their causes:

**Bacteria.**—A bacterial invasion of the cornea frequently occurs, especially following injury. Prompt treatment with suitable antibiotics is effective in most cases.

**Fungus.**—Long-term antibiotic and steroid therapy may have increased the incidence of fungal overgrowths which produce corneal ulcers. Fungi may also invade the eye through eye solutions which are not sterile. Anti-fungal drugs are effective in some cases.

**Viruses.**—The most common cause of corneal ulcers and blindess is infection with a virus called *herpes simplex,* which also causes the common cold sore. Like other viruses, it does not yield to treatment with the common miracle drugs (antibiotics, antifungicides, sulfa drugs, and corticosteroids). It is not surprising, then, that the medical world hailed the discovery by an Institute grantee that herpes simplex virus of the cornea could be treated with an antimetabolite developed to treat cancer. The new weapon, 5-iodo-2-deoxyuridine, or IDU for short, represented the first known cure for a virus disease. Since that time IDU, and similar drugs which were developed later, have cured thousands of cases of corneal herpes simplex.

Corneal ulcers due to a virus called variola were common before smallpox vaccination was available. They still occur in underdeveloped areas of the world where vaccination is not practiced.

Infection with *vaccinia* virus is occasionally seen as an accidental complication of smallpox vaccination. Prevention of secondary bacterial infection is the only treatment.

**Allergic reaction.**—By far the most common corneal ulcers are thought to be the result of an allergic reaction to certain types of infection. Steroid therapy is usually effective.

**Death of nerve supplying cornea.**—Death or injury to the fifth cranial nerve sometimes renders the cornea unable to defend itself against infections and ulcers. Because there is no way of repairing the nerve at present, the condition is difficult to treat.

**Exposure.**—If not properly moistened and covered by the eyelids, the cornea is subject to minor injuries and drying which foster the development of ulcers. This can be prevented by artificial moistening.

**Corneal Dystrophies.**—The corneal dystrophies are a rare group of slowly progressive noninflammatory degenerative disorders which affect both eyes and usually appear in the second and third decades of life. Some are hereditary. Other cases follow ocular diseases and some are of unknown cause.

*Plastic implant sometimes replaces scarred cornea. (Columbia University)*

## corneal transplants

When corneal diseases are not treated promptly, they may destroy the cornea's transparency, thereby blocking the passage of light and resulting in poor vision or blindness. Fortunately, in such cases corneal transplant operations can sometimes restore sight by substituting a healthy cornea for the diseased one. Knowledge of corneal transplant operations often leads to the belief that the whole eye can be replaced; this is not true.

Until recently, the cornea was the only part of the body which could be replaced by tissue from another person, the reason being that the cornea has no blood vessels and therefore fewer immune reactions to foreign tissue are set up by the transplant.

**Preserved Corneas.**—Successful corneal transplants have been common for almost 20 years. They are usually performed with corneas taken posthumously from persons who have previously signed statements donating their eyes to eye banks. In 1956, an Institute grantee and his research team developed a process for dehydrating and preserving the cornea removed from the eye of a deceased donor. This was an invaluable step in aiding countless blind people, for while fresh corneas must be used shortly after removal from a donor, the preserved corneas can be kept indefinitely, shipped anywhere, and then rehydrated and made ready for grafting in a few minutes. However, preserved corneas are only usable for lamellar or partial-thickness transplants, and about half of all corneal operations require full-thickness transplants, for which fresh tissue is required. Research may soon make it possible to quick-freeze corneas and still use them for full-thickness transplants.

**Research.**—Corneal tissue is being studied by research workers to discover why the transplant sometimes becomes cloudy several months after the operation. The clouding appears to be partly due to an immune reaction of the eye to foreign tissue, and to other factors such as temperatures used in freezing and storing, the rapidity with which the corneas are thawed, and the effect of glycerin or other products used in preservation.

Many blind persons still cannot benefit from a corneal transplant operation, either because of a scarcity of donor material or because the cornea is so densely scarred, it will not accept the graft. In these patients repeated grafts fail because of formation of blood vessels in the cornea or swelling from allergic response to the graft. For some such individuals new hope is offered in the form of plastic implants to replace scarred corneas. Synthetic corneas were attempted a century ago, but it was not until the development of newer plastics that a material was found to which the eye did not set up an allergic reaction. Although further studies are necessary to determine whether such implants are permanently successful, a few patients have had their sight restored by these small plastic discs replacing natural cornea.

# uveitis

Between 7 and 15 percent of all blindness in the United States is caused by an inflammatory disease of the eye called uveitis. Approximately 2,000 persons each year lose their sight because of this condition and twice that number suffer impairment of vision.

Treatments can benefit persons afflicted with uveitis in many cases.

## anatomy

Uveitis affects the eye's uveal tract, which includes the iris, the ciliary process, and the choroid.

The *iris* is the colored part of the eye which controls the amount of light entering it.

The *ciliary body* is a series of tiny muscles controlling the size of the lens, accommodating it to close or distant objects. It is located out of sight, just beyond the iris. It also contains the secretory organ, the ciliary process, which produces eye fluid.

The *choroid,* the middle layer of the eye, runs into the iris and ciliary body. It is a network of blood vessels which supplies the retina.

## what is uveitis?

When the inflammation occurs in the choroid, uveitis is usually of the granulomatous type. Without beneficial treatment, the disorder may last from months to years causing permanent damage and marked loss of vision.

*Photo: Staining solutions color some tissues of the eye for better identification under the microscope.*

When inflammation occurs in the iris or the ciliary body, uveitis is most frequently *nongranulomatous*. With treatment, this painful disorder may last only a few weeks, although it may recur with eventual damage to vision.

## symptoms

Granulomatous uveitis may produce gradual blurring of vision, a reddening of the eye, minor pain, some degree of intolerance to light, and an irregular pupil.

In nongranulomatous uveitis intolerance to light and blurred vision are more pronounced. The pupil is small.

## what causes uveitis?

Granulomatous uveitis can be caused by an invasion of the eye by microbes which are sometimes associated with a variety of other diseases. About 30 percent of all uveitis cases are thought to be caused by toxoplasmosis, an inflammation caused by a protozoan parasite.

Tuberculosis, sarcoidosis (a disease leaving sores in many parts of the body), syphilis, and perhaps amoebic dysentery and histoplasmosis (a fungus infection) may also cause granulomatous uveitis.

Nongranulomatous uveitis is of unknown cause. Some scientists think that it might be an allergic reaction or an auto-immune disease, that is, a sensitization of the tissues of an individual's eye to something in his own body.

## treatment

If possible, the underlying condition which caused granulomatous uveitis disorder is treated. Because it is difficult to determine which microbe is responsible for the infection, many laboratory tests are necessary. However, if no cause can be discovered, drugs are given which abate the inflammation.

Nongranulomatous uveitis usually responds to treatment of the eye itself. Local steroid drops may reduce the inflammation and combat the allergic reaction. A drug, atropine, prevents the iris from sticking to other eye parts. Warm compresses can be applied, and pain killers used. Dark glasses protect overly sensitive eyes from light.

## complications

Because the uveal tract extends around almost the whole eyeball any inflammation of it easily disturbs nearby tissues. The choroid lies so close to the retina that granulomatous uveitis often affects the retina, causing chorioretinitis. Cataracts and retinal detachment may result. Both are difficult to treat when the eye is inflamed. Any form of uveitis may cause cataracts and glaucoma.

## research

Research into uveitis takes two main courses: to uncover all of the infectious agents which cause granulomatous uveitis and develop treatments; and second, to determine whether nongranulomatous uveitis is, indeed, an autoimmune disease.

New techniques enable scientists to gather precise information about different reactions involved in uveitis. In one test, particles are labeled with a material which makes them visible in fluorescent light. Scientists can observe what happens when they combine with other particles in the uveal tract.

Uveitis caused by toxoplasmosis is being investigated extensively. Recently, scientists at NINDB found evidence that harmful side effects produced by daraprim, a drug used to treat toxoplasmosis, can be eliminated. Although the drug does not prevent relapses, it can reduce destructive changes in the eye in many instances.

In another experiment, the uveal tissue of rabbits and guinea pigs is being made hypersensitive. Investigators want to know if antibodies are present. If they are, granulomatous uveitis may possibly be an autoimmune disease in which the eye responds with the production of antibodies to its own slightly altered tissues. The excessive antibody production results in inflammation.

# trachoma

Trachoma, although not a large problem in the United States as a whole, is still prevalent among Indians and Mexicans in southwestern United States. In the world generally it is still the leading cause of blindness. Trachoma is a chronic disease of the cornea and conjunctiva leading to corneal scarring. It spreads in families and is encouraged by poverty and poor hygiene. The disorder can be cured by drugs, but there is a lack of natural immunity and frequent reinfection is common.

Trachoma affects the eye's conjunctiva, a membrane which lines the eyelids and covers the front portion of the eye. In severe cases the infection may spread to the cornea, the transparent coating of the eye, reducing vision to light perception only. Both eyes are usually affected.

## what is trachoma?

Trachoma is an infectious disease. It spreads by direct contact. The conjunctiva becomes thickened, swollen, and inflamed. Follicles (a word derived from a Latin term meaning "small bag") appear on the inner side of the eyelid. When the disease begins to heal, the follicles disappear and scar tissue forms. During the process the cornea may be invaded by blood vessels and granulation, resulting in corneal scarring and loss of vision. A new research finding indicates that this occurs only in people who have previously been infected by the trachoma virus.

## symptoms

Signs of trachoma include an intolerance to light, tearing, a burning sensation, and the feeling of something caught in the eye.

## what causes trachoma?

Trachoma is caused by a viruslike infection called "chlamydia trachomatis." All ages are affected.

Trachoma is easily spread because anything touching an infected eye can pass the disease. When many people use the same towel, trachoma may spread easily from one to another.

Trachoma agents have been isolated in the genital tract as well as the eye. Some scientists believe that a genital infection in the mother may cause a trachomalike disease in the eyes of her newborn child, called inclusion blennorrhea.

## treatment and research

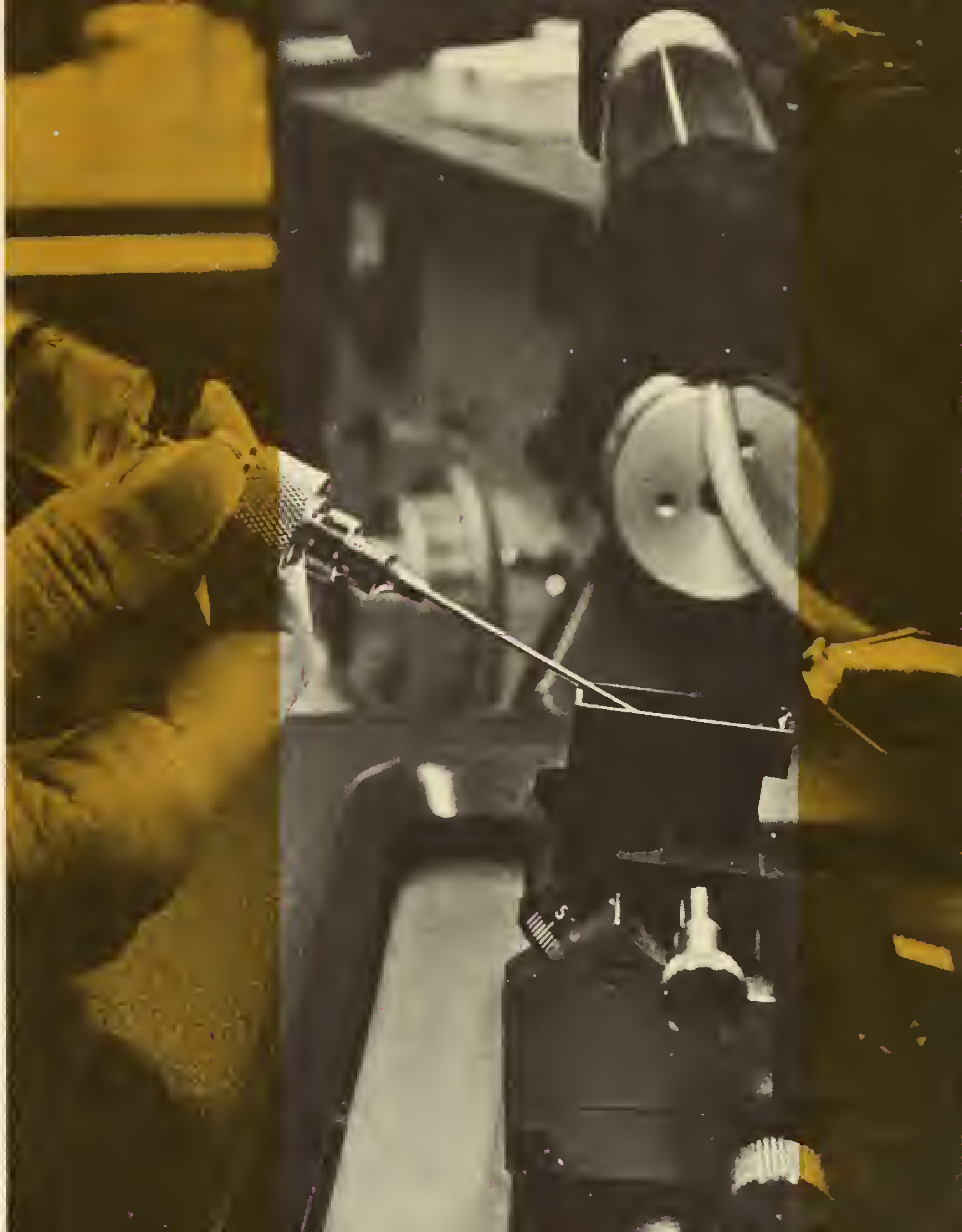
Several drugs are used to treat trachoma and its complications. When drugs are given early, the disease may be arrested without extensive damage to the eyes. However, the only safe and practical method presently available for mass treatment is local use of a sulfa ointment. Unfortunately, this treatment takes a long time. Drugs which act more rapidly than sulfa are needed.

Prevention is the best form of treatment. Personal hygiene is extremely important. Individual sleeping arrangements, and individual washcloths and towels keep trachoma from spreading. A person who has been cured of trachoma may be reinfected by new exposure to the disease. Studies show that damage to the eye, resulting from a hypersensitivity phenomenon, occurs only after reinfection.

Scientists are trying to discover ways of killing the trachoma agent. Heat and drying are effective. Soap, however, may not be entirely effective for preventing multiplication of the virus.

Since the trachoma virus was first isolated in 1957, Institute grantees have been working to develop effective vaccines. Years of research eventually produced favorable results, but there remains the problem of vaccine-induced infections in some humans and monkeys. Research is continuing at several laboratories throughout the world. A relatively easy way to produce high potency vaccine is still to be developed.

The outlook for trachoma research is excellent. There is good reason to believe that with massive trachoma inoculation or improvements in sanitation, the disorder will vanish or diminish greatly within the next several decades.



*A syringe is used to add fluid to container to float delicate sections cut by the microtome.*

# refractive errors

## light entering the eye

Centuries of studying optics and the behavior or light entering the eye have given scientists a comprehensive knowledge of refractive errors and how they can be corrected with eyeglasses. These studies have shown that light entering the eye is refracted (bent) by the cornea and that the lens acts as an automatic focusing device. Objects at different distances are each, in turn, sharply focused. A contraction of the ciliary muscle brings about the relaxation of the fibers which support the lens. This, in turn, allows the elastic lens capsule to mold the lens so that its front surface bulges forward in the center. This action increases the refractive power of the eye and enables it to see a nearby object clearly. The process is reversed when the eye looks from a near to a distant object.

## near sightedness and far sightedness

If the eyeball is too long, the image tends to be focused in front of the retina instead of on it as in a normal eye. In this case, only nearby objects can be seen clearly and the person is said to be nearsighted or myopic. The opposite condition, where the person sees only distant objects clearly, is known as hyperopia or farsightedness. Astigmatism results from an uneven curvature of the cornea.

Most of these conditions can be corrected with eyeglasses, which compensate for the refractive error in the eye. But eyeglasses at best are a nuisance. They block out much side vision; they hamper participation in sports and other activities, and they make their wearers dependent upon an item that may be broken, lost, or become outdated. Many persons have difficulty getting a prescription for eyeglasses that enables them to see comfortably and clearly. Scientists therefore continue to seek better means of detecting and correcting refractive errors. Contact lenses are a help to some, but others cannot wear them, either because of a condition in their eyes or because they cannot adjust to them.

## presbyopia

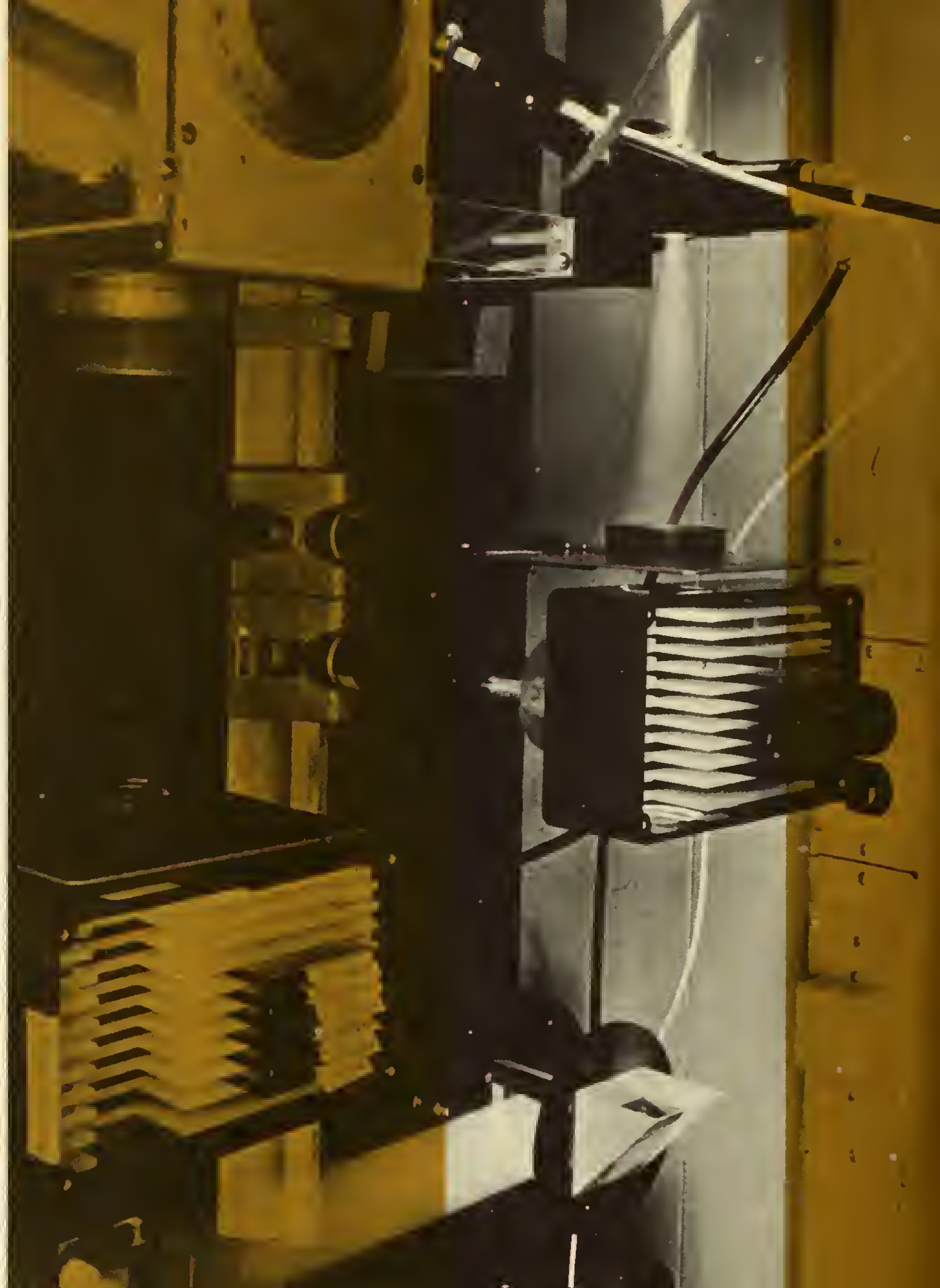
As a person ages, the ability of the eye to change its focus to different distances gradually wanes. By the mid-forties, the accommodative power has usually dwindled so much that it is impossible to read or do close work for a prolonged period without bifocals or reading glasses. This condition is called presbyopia, and affects almost everyone who lives long enough.

## myopia

Of the other defects of focus—myopia, hyperopia, and astigmatism—*myopia* is by far the most troublesome. It accounts for 2 percent of the blindness in the United States. It is most often caused by the largeness of the eyeball, but may also be affected by the focusing power of the cornea or lens. In many instances, myopia of moderate degree develops during youth and comes to a standstill or increases only slightly after puberty. Another type, called "stationary" or "simple" myopia, causes a very limited increase up to the 20th year. In other cases, the error reaches a considerable height in youth and increases steadily up to the 25th year or even later, resulting in a high degree of myopia. This type, known as "progressive" myopia, may be accompanied by destructive changes in other parts of the eye and usually leads to serious impairment of vision. Extreme cases result in blindness.

## research on refractive errors

Studies of the visual perception of time, space, color, brightness, acuity, and form continue to provide new insights, but new techniques have extended their application and meaningfulness. High-speed computers and ultrasound measurements have provided a completely new approach to the study of refractive errors. These new techniques provide a far greater precision than would have been dreamed of by conventional methods. Their application may enable scientists to resolve the age-old controversy of whether myopia is completely hereditary or whether it may be affected by a large amount of close work and by other environmental factors.



*Instruments for recording electrical impulses from the retina.*

# amblyopia ex anopsia

## nonuse of one eye

Amblyopia ex anopsia is a dimness of vision without pathologic defect in the retina, optic nerve, or visual pathway. It may exist at birth or be acquired soon afterwards and develops under circumstances leading to nonuse of one eye. The condition may be due to muscular imbalance, refractive error, or other defect present when the infant is still learning to focus his eyes. For example, the child may see a double rather than a single image. When his attempts fail to get these two separate pictures to come together, he tends to suppress the weaker eye and use only the stronger one. When this becomes a habit, the vision in the weaker eye is gradually lost or fails to develop properly.

## treatment in children

Correction of amblyopia in the young traditionally consists of placing the good eye at an optical disadvantage and forcing the child to use the amblyopic eye. This may be done by patching the good eye, by exercises, or by blurring the retinal image of the sound eye through the use of eye drops.

## early discovery important

If amblyopia is discovered before the age of three, treatment is often successful. Between the ages of three and six, there is still a good chance of success, but after age six, present treatment has brought improvement for only a small percentage of cases. Therefore, the greatest hope for this disorder lies in early discovery. However, even with increased alertness for amblyopia in young children, there will continue to be cases which remain undiagnosed until it is too late to treat them by conventional means.

## understanding the defect

For this reason, scientists would like a clearer insight into the nature of the processes leading to amblyopia. They believe that significant progress in the treatment of amblyopia will have to await a more thorough understanding of the normal mechanisms of vision from the absorption of light by the retina to the interpretation of a visual message in the brain. The ERG (electroretinogram) and related clinical tests are helping scientists to determine whether the defect in a particular person lies in the eye itself or in the nerve pathway of the brain behind the eye.

Much of the work of the Institute grantees has been directed to mapping the visual impulse through the retina and various nerve pathways in the brain. The knowledge that has been gained from these studies has contributed greatly to understanding of the nervous system, as well as the visual function. It has been shown, for instance, that there is an independent nerve pathway for the eye to pick up and follow moving objects.

# eye injuries and tumors

Despite the protection afforded the eye by its location within a strong protective bony structure, serious injuries to the eye are more frequent than is often realized. During wartime, eye injuries constitute approximately 5 percent of the hospital admissions for battle injuries and 10 percent of the accidental noncombat-incurred injuries.

In today's modern hospital, improved surgical techniques and new drugs supplement the body's natural defenses in restoring healthy functioning to an injured eye. Such treatment has been made easier by research on changes which take place during the normal healing process. One group, for instance, studied enzyme changes following trauma to the eye.

## wound healing

Wound healing in the cornea (the transparent membrane over the colored part of the eye) has been investigated because it is often during the healing process that the cornea becomes scarred and opaque. When this happens the person is blind unless a successful corneal transplant operation can be performed.

Specific cells in the cornea have been found important in the process of wound healing. At the junction of the cornea and the adjacent tissue, the sclera, these cells (called mast cells) form a barrier to the formation of blood vessels in the cornea. (Unlike most body tissue, the cornea is normally transparent and free of blood vessels.) In injury, however, the barrier is broken, permitting the blood vessels to grow across the cornea. This formation of blood vessels makes the healing process more analogous to that in other parts of the body, and often leads to permanent opacities of the cornea. (See section on Disorders of the Cornea.)

## retinal burns

The atomic age has created additional vision hazards because of exposure to light of high intensity. Research has attempted to characterize damage from atomic explosions in order to make some degree of protection possible. Studies have shown that the size of the pupil more than the distance from the blast determines whether or not an individual retina is burned. For example, a 20 kiloton nuclear weapon can produce a retinal burn in human subjects who are at least 36.3 miles from a detonation during the day and 40 miles at night. Astronauts are subject to retinal burns because of their comparative closeness to the sun and the absence of atmosphere filtration.

Retinal burns from the sun, like those from atomic bombs, are due to the thermal effect of the visible and near infrared rays focused on the pigment structures behind the retina. The normal eye can tolerate fleeting glances at the sun, but as Socrates learned from others, and as Galileo discovered for himself, it will not permit prolonged solar observation.

Nevertheless, eclipses of the sun continue to produce retinal burns in unsuspecting persons who either are not aware of the danger or who fail to take proper precautions. Colored glasses, smoked glasses, and exposed photographic film are commonly used (also pinholes, broken beer bottles, and other common objects at hand), but the effectiveness of these filters varies so widely that they are not recommended. Moreover, in a recent report from Australia where 170 persons had ocular damage from observing the eclipse of 1959, many of the injured had used these filters—and some had viewed the eclipse for as short a period as 10 seconds.

Just before eclipse of the sun in 1963, the American Medical Association warned, "Don't look at the eclipse unless you have first obtained expert guidance on how to do it without injuring your eyes."

Most people, especially children, don't realize that less than one second's exposure to the direct rays of the sun can, under some circumstances, cause permanent loss of central vision. There is no pain when the damage is done.

The danger in eclipse-viewing is that the eclipse blocks out visible rays, which usually deter people from gazing into the sun, but fails to block infrared rays, which are just as harmful.

## chemical burns

Medical advice should be sought promptly when the eye is injured in any way. Early treatment may save vision. When a chemical or other irritant is splashed into the eye, it is best to irrigate quickly with warm tap water for about 5 minutes. Do not try to neutralize an acid or alkali by using its chemical counterpart, as the heat generated by the reaction may lead to further damage. If the chemical irritant is an alkali, the irrigation should be continued for at least half an hour. Examination should be made by a physician to avoid complications.

## foreign bodies

Foreign bodies, if allowed to remain under the eyelid, can cause injury by scratching the cornea. They may also be lodged in the cornea. An eye physician has special instruments and techniques to detect foreign bodies the patient may be aware of only through pain or irritation. He may also instill an anesthetic to relieve pain. When the foreign body penetrates the outer coats of the eye and is retained within the eye, various complicated procedures are employed to locate the foreign body and to remove it. One new technique for location of foreign bodies consists of the use of ultrasonic echoes bounced off the dense particle in the eye.

# the future

We communicate with the outside world through our senses. Without them we would be isolated from one another and from our environment. In man, vision is by far the most important of the senses; some 38 percent of all sensory input to the brain is mediated through the structures which comprise the visual system. Thus, blindness is devastating for any individual; and a thorough understanding of the visual process is important, not only for the cure of diseased eyes but also to anticipate and prevent eye disease.

Scientists are justly proud of the research gains that have been made, and they are optimistic about the added cures and knowledge which will come from future research.

*The frog and horseshoe crab are among laboratory animals studied to understand eye disorders.*

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